REMARKS

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

The rejection of claims 1-34 under 35 U.S.C. § 112 (2nd paragraph) as being incomplete for omitting essential steps is respectfully traversed.

By the above rejection, the U.S. Patent and Trademark Office ("PTO") is requiring that the present claims be limited to preferred embodiments taught in the specification. Yet, it is well-known that a claim need not be so limited. *Gentry Gallery, Inc. v. Berkline Corp.*, 134 F.3d 1473, 1479 (Fed. Cir. 1998) ("It is a truism that a claim need not be limited to a preferred embodiment."); *SRI Int'l v. Matsushita Elec. Corp.*, 775 F.2d 1107, 1121 (Fed. Cir. 1985) (en banc) ("If everything in the specification were required to be read into the claims, or if structural claims were to be limited to devices operated precisely as a specification-described embodiment is operated, there would be no need for claims. Nor could an applicant, regardless of the prior art, claim more broadly than that embodiment. Nor would a basis remain for the statutory necessity that an applicant conclude his specification with 'claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.'" (citing 35 U.S.C. § 112")); *Reiffin v. Microsoft Corp.*, 214 F.3d 1342, 1348 (Fed. Cir. 2000) (Newman, J. concurring) ("Section 112 P2 instructs the applicant to 'distinctly claim[] the subject matter which the applicant regards as his invention.' This does not automatically require inclusion in every claim of every element that is part of the device or its operation. . . . When the claim is supported by the patent's disclosure, is adequately distinguished from the prior art, and otherwise meets the statutory requirements of patentability, neither law nor policy requires that the claim contain all the elements described in the specification as part of the . . .method.").

The requirement under 35 U.S.C. § 112 (2nd paragraph) that the claims particularly point out and distinctly claim the invention merely requires that the claims be clear to a person of ordinary skill in the art. *Orthokinetics, Inc. v. Safety Travel*, 806 F.2d 1565, 1576 (Fed. Cir. 1986) ("A decision on whether a claim is invalid under § 112, 2d para., requires a determination of whether those skilled in the art would understand what is claimed when the claim is read in light of the specification."). The claimed methods of detecting a neurodegenerative disease in a mammal and producing an image of brain tissue from a mammal are clear. In fact, the PTO has made no assertion in any of its office actions that the claims would not be understood by a person of ordinary skill in the art.

The outstanding office action fails to address any of these arguments and simply maintains the rejection on the basis that essential steps have been omitted, citing the Manual of Patent Examining Procedure ("MPEP") § 2172.01. However, this section of the MPEP only suggests making a rejection under 35 U.S.C. § 112 (2nd para.) where "a claim fails to interrelate essential elements of the invention". Here, there is no suggestion in the outstanding office action that the claims fail to interrelate the claimed steps. In the absence of such circumstance, MPEP § 2172.01 in no way authorizes a rejection under 35 U.S.C. § 112 (2nd para.).

In any event, although not required to further limit the claims to satisfy 35 U.S.C. § 112 (or 35 U.S.C. § 101 (discussed *infra*)), applicants have amended the claims as an accommodation and to reduce issues. Specifically, amended claim 1 is directed to a method of detecting a neurodegenerative disease in a mammal. This method involves activating brain tissue of the mammal by application of radiation through an opening or a thinned portion of the mammal's skull under conditions effective to promote a simultaneous multiphoton excitation of the brain tissue and to emit a fluorescence characteristic. The radiation has a wavelength in the visible red to the infrared region of the light spectrum and is pulsed at a pulse width between about 10^{-9} to 10^{-15} second. The fluorescence characteristic is compared to a standard fluorescence emitted by exciting healthy brain tissue of the mammal under the same conditions used to carryout the activating. Brain tissue where the fluorescence characteristic differs from the standard fluorescence is identified as having a neurodegenerative disease.

Claim 19, as amended, is directed to a method of producing an image of brain tissue from a mammal. This method involves activating brain tissue of a mammal with radiation applied through an opening or a thinned portion of the mammal's skull under conditions effective to promote a simultaneous multiphoton excitation of the brain tissue and to produce a fluorescence. The radiation has a wavelength in the visible red to the infrared region of the light spectrum and is pulsed at a pulse width between about 10^{-9} to 10^{-15} second. The fluorescence is collected to produce an image of the brain tissue.

Support for the amendments to claims 1 and 19 is found in the present application, as filed, at page 11, lines 6-7, page 13, lines 17-28, and in original claims 6-7, 15-16, 22-23, and 31-32. Support for new claims 39 and 40 is found in the present application, as filed, at page 11, lines 6-7.

Accordingly, the rejection of claims 1-34 under 35 U.S.C. § 112 (2nd paragraph) should be withdrawn.

The rejection of claims 1-34 under 35 U.S.C. § 101 for lack of utility is respectfully traversed.

Compliance with 35 U.S.C. § 101 requires that the written description provide a credible assertion of specific and substantial utility of the claimed invention. *Brenner v. Manson,* 383 U.S. 519 (1966). As stated throughout the specification, the present invention is directed to detecting a neurodegenerative disease and imaging brain tissue using multiphoton excitation. Given the success of the experiments carried out in the Examples, one of ordinary skill in the art would find the usefulness of the claimed invention credible. With the pending specification completely satisfying the standard of *Brenner v. Manson*, there is no basis for requiring that the claims be amended and the outstanding office action does not provide any basis for making a rejection under 35 U.S.C. § 101 where the disclosure of the application meets this standard. Indeed, the outstanding office action is fundamentally flawed in that the rejection under 35 U.S.C. § 101 is premised on "the disclosed invention [being] inoperative". At no time have applicants ever said this and there is no basis in the outstanding office action for such a position. While applicants have asserted that Christie et al., "Multiphoton Imaging of Alzheimer's Disease Neuropathology," *Society for Neuroscience Abstracts* 24(1-2):1219 (1998) ("Christie") lacks important features, those deficiencies are clearly obviated by the disclosure of the present application.

For all of these reasons, the rejection of claims 1-34 under 35 U.S.C. § 101 for lack of utility should be withdrawn.

The rejection of claims 1-34 under 35 U.S.C. § 112 (1st paragraph) for lack of enablement is respectfully traversed.

The specification fully enables a person of skill in the art to practice the claimed methods without undue experimentation. In particular, conditions effective to promote a simultaneous multiphoton excitation of brain tissue by application of radiation may be carried out, according to one preferred embodiment, by thinning (e.g., drilling or abrading) the mammal's skull (page 11, lines 5-6) or, in an alternative embodiment, by performing a craniotomy (page 11, lines 6-7). Suitable wavelengths by which activation of brain tissue is carried out are also specifically taught as are various preferred power levels and pulse durations (page 13, line 17 to page 15, line 5). Preferred embodiments of how low energy

photons are to be summed are also specifically taught by the present application (page 12, line 24 to page 13, line 16).

The enablement requirement of 35 U.S.C. § 112 (1st paragraph) is satisfied by what is disclosed in the specification and not by what is found in the claims:

> That claims are interpreted in light of the specification does not mean that everything expressed in the specification must be read into all the claims. On the contrary, as was said in *Environmental Designs, supra,* 713 F.2d [693,]...699, 218 *USPQ* [865,]...871 [(Fed. Cir. 1983)]:
>
> > the specification must be sufficiently explicit and complete to enable one skilled in the art to practice the invention, while a claim defines only that which the patentee regards as his invention. *35 U.S.C. § 112.* The claim, not the specification, measures the invention. (Case cited). The argument that claim 1 must include a limitation found in the specification is thus legally unsound. *Smith v. Snow* 294 U.S. 1, 79 L. Ed. 721, 55 S. Ct. 279 (1935).

Raytheon Co. v. Roper Corp. 724 F.2d 951, 957, 220 USPQ 592, 597 (Fed. Cir. 1983). In view of the subject matter disclosed in the specification of the present application, it is clear that the present application is enabling.

A rejection under 35 U.S.C. § 112 (1st paragraph) for lack of enablement on the grounds that a critical limitation is absent from the claims is only proper when the specification clearly states that the limitation is a critical feature of the invention:

> Limiting an applicant to the preferred materials in the absence of limiting prior art would not serve the constitutional purpose of promoting the progress in the useful arts. Therefore, an enablement rejection based on the grounds that a disclosed critical limitation is missing from a claim should be made only when the language of the specification makes it clear that the limitation is critical for the invention to function as intended. Broad language in the disclosure, including the abstract, omitting an allegedly critical feature, tends to rebut the argument of criticality.

MPEP § 2164.08(c). The disclosure in the specification clearly satisfies this standard by generally describing the present invention and identifying a number of alternative embodiments for carrying out the claimed methods. Therefore, the claims need not be limited to these embodiments.

The outstanding office action fails to respond to these points which were also set forth in the July 26, 2005, Amendment. Instead, it simply maintains the rejection based on *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). However, *Mayhew* is no longer on point in view of the above amendments.

Since the present application fully enables the claimed invention, the rejection of claims 1-34 under 35 U.S.C. § 112 (1st paragraph) should be withdrawn.

The rejection of claims 1-34 under 35 U.S.C. § 103(a) for obviousness over U.S. Patent Publication No. 2002/0115717 to Gervais et al., ("Gervais") in view of U.S. Patent No. 6,280,386 to Alfano et al. ("Alfano") and Christie is respectfully traversed.

Gervais relates to the use of amyloid-targeting imaging agents for imaging amyloid plaques *in vivo*. The amyloid-targeting imaging agents include an amyloid targeting moiety linked to a labeling moiety. The targeting moiety localizes the imaging agents to amyloid plaques, and the labeling moiety allows the imaging agents to be visualized by ultrasound imaging, computed tomography imaging, magnetic resonance imaging, nuclear medicine imaging, optical imaging, and elastography. Labeling moieties taught by Gervais for use in optical imaging include fluorescent or colored dyes. There is no suggestion in Gervais of using simultaneous multiphoton excitation, as claimed.

Alfano teaches an imaging system in which images of objects within tissue are enhanced by applying a contrast agent to a sample to be imaged, thereby forming a luminous object. The tissue is illuminated and 2 image signals are recorded. These 2 image signals are subtracted to minimize an image component resulting from the tissue and to enhance the image component resulting from the luminous object. Alfano also fails to suggest the use of simultaneous multiphoton excitation.

The use of simultaneous multiphoton excitation in accordance with the present invention has a number of very important benefits. In particular, multiphoton excitation has a very high resolution capability, on the order of one micrometer (page 20, lines 26-29 of the present application), and can reach unprecedented depths (page 27, lines 15-18 of the present application). In addition to permitting high resolution imaging of living tissue, multiphoton excitation has the unique advantage of incurring only minimal photodamage or toxicity on the living tissue being imaged (page 25, lines 25-26 of the present application). These unique features of multiphoton excitation imaging make possible the detection and observance of certain Alzheimer's Disease-like lesions that are otherwise undetectable with prior art imaging technologies (page 25, lines 21-25 and page 46, lines 11-12 of the present application). Multiphoton excitation methods of imaging also provide the opportunity to evaluate a relatively large 3-dimensional reconstruction of the cerebral vasculature (page 32, lines 17-19 of the present application). Additionally, multiphoton excitation of fluorophores provides a method of imaging with improved background discrimination and reduces

photobleaching of the fluorophores (page 12, line 19 to page 13, line 8 of the present application).

Christie is cited to disclose the use of multiphoton imaging to analyze Alzheimer's Disease neuropathology. As set forth in the Declaration of Watt W. Webb Under 37 CFR § 1.132, which accompanied the Request for Reconsideration mailed September 7, 2004 ("Webb Declaration"), Christie begins by citing a number of advantages if this approach were to be successful ("Webb Declaration") ¶ 7). However, Christie does not provide an enabling disclosure of the present invention.

Moreover, neither Gervais, Alfano, nor Christie teach application of radiation through an opening or a thinned portion of the mammal's skull, where the radiation has a wavelength in the visible red to the infrared region of the light spectrum and is pulsed at a pulse width between about 10^{-9} to 10^{-15} second.

As a result of all of these deficiencies in the cited references, the rejection of claims 1-34 for obviousness over Gervais in view of Alfano and Christie is improper and should be withdrawn.

In view of the foregoing, applicants submit that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

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